REMARKS

In accordance with the above amendments, claims 1, 4, 7, 9-13, 17, 20, 23, 32, 34-35 and 37-40 have been amended, claim 21 has been canceled and new claim 45 has been added. Thus, claims 1-20, 23 and 32-45 remain under consideration.

It is noted that claim 23 is objected to, but it is not otherwise rejected and, therefore, is assumed to be of an allowable scope.

With respect to formalities, it is first noted that claim 5 is objected to under 37 CFR § 1.75(c) as being in improper form. This rejection is respectfully traversed. Note that claim 5 is dependent on any one of claims 1-3 and none of claims 1-3 are multiple dependent claims. Therefore, claim 5 is believed to be proper and applicant respectfully requests that this objection be withdrawn.

It is noted that claim 22 stood rejected under 35 USC § 112, second paragraph, as being indefinite. That claim has been rewritten as claim 45 which should be in proper form.

It is noted that claim 32 has been rejected under 35 USC § 112, second paragraph, as being indefinite. That claim has also been rewritten to eliminate specific product names and so it should no longer be subject to the present rejection.

It is noted that claims 33-39 have been rejected under 35 USC § 112, second paragraph, for using trademark names. This

rejection is not understood inasmuch as claims 33-39 contain no trademarks or trade names and it is not seen how they can be indefinite. The use of the acronym "TMOS" has been defined in claim 34 as tetramethyl ortho silane as defined at page 4, line 28, of the specification. Thus, these claims should now be considered definite and this rejection should also be withdrawn.

With respect to the merits of the claims, claims 1-4, 6-9, 12, 14-17 and 40-44 stand rejected under 35 USC § 103(a) as being unpatentable over Stevens (CURRENT OPINION IN STRUCTURAL BIOLOGY, *High-Throughput Protein Crystallization*, Vol. 10, (2000), pp. 558-563). Stevens is cited as teaching a method for automatically crystallizing protein using microbath and sitting or hanging dropped vapor diffusion. An automatic liquid dispensing system using two robotic crystallization systems within emersion oil to cover over the micromolecules is also disclosed. This rejection is respectfully traversed as applicant believes that important and patentable differences exist between what Stevens teaches or suggests and the present claims.

Stevens presents a review of methods used for automated and high-throughput protein crystallization. That review was published shortly before the priority date of the present application and can be considered as reflecting the state of the art at the time the present invention was made. While a number of different methods are reviewed in Stevens (2000), in each

case, no mention or suggestion is made that it would be advantageous to include a gel-forming component in the crystallization trials. Stevens, in fact, is completely silent on using a gel-forming component in the crystallization trial.

In this regard, D'Arcy et al (J. CRYSTAL GROWTH, *A Novel Approach to Crystallising Proteins Under Oil*, Vol. 168, (1996), pp. 175-180) is also cited as teaching a similar method for crystallizing proteins and other biological macromolecules under paraffin oil-containing silicon utilizing various volumetric samples. While D'Arcy et al does report a method for crystallizing proteins under oil, here also it should be noted that none of the oils used in D'Arcy et al (1996) act as a "gel-forming component": the oils do not form gels, instead they function to regulate the diffusion of water molecules from the crystallization experiment to the oil-air interface. D'Arcy et al (1996), like Steven (2000), is also completely silent with respect to using a gel-forming component in protein crystallization experiments.

Thus, neither Stevens (2000) or D'Arcy et al (1996) suggest using a gel-forming component in automated crystallization trials. Contrary to the Examiner's view, in fact, the skilled person would not have attempted to use a gel-forming component in an automated method of optimizing crystallization conditions since it would have been expected that the resulting gel would

have formed in the automatic liquid dispensing system and hence would have clogged the fine dispensing tips used by such machines.

Thus, not only do the cited references not teach or suggest the use of a gel-forming component in a protein crystallization experiment, if anything, they teach away from attempting to use such a component based on the known limitations of the experimental equipment. Thus, applicant submits that the use of gel-forming component cannot reasonably be inferred from the cited references and the beneficial results clearly are surprising and quite unexpected as indicated on page 5 of the present application. This is believed to be clear evidence of unobviousness.

In view of the above amendments, taken together with the remarks herein, applicant submits that the skilled person would not have been motivated to adapt the teachings of Stevens (2000) and/or D'Arcy et al (1996) to arrive at the present claims. Accordingly, applicant requests that the present rejections be withdrawn and the claims allowed.

Should issues remain which, in the opinion of the Examiner, could be resolved by telephone interview, she is asked to contact the undersigned attorney at her convenience to discuss and

resolve same in an effort to expedite prosecution of this application.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE

I hereby certify that the foregoing Amendment in response to the Official Action mailed February 21, 2006, in application Serial No. 10/680,390, filed on October 2, 2003, of Naomi E. Chayen, entitled "METHODS OF CRYSTAL OPTIMISATION", and a Transmittal Letter are being sent by facsimile transmission to: The Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 16, 2006.

Barbara L Davis

Barbara L. Davis
On Behalf of C. G. Mersereau

Date of Signature: May 16, 2006